STATEMENT
OF
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ON
OVERSIGHT OF RESEARCH AND OTHER ISSUES
BEFORE THE
SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS
AND THE
SUBCOMMITTEE ON HEALTH
OF THE
COMMITTEE ON VETERANS' AFFAIRS
U.S. HOUSE OF REPRESENTATIVES

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Mr. Chairman and Members of the Subcommittees, thank you for the opportunity to appear before you to discuss the activities of the Office of Research Compliance and Assurance (ORCA) and, in particular, its role and responsibilities in the protection of human research subjects in the Veterans Health Administration (VHA). Further, this will provide an update on the scope, structure, philosophy, and product lines of ORCA since this committee's oversight hearings of April 21, 1999, and September 28, 2000.

Scope

The scope of ORCA is defined in the Mission statement, which is in accordance with the commitment made to the Congress in 1999:

> The Office of Research Compliance and Assurance (ORCA) serves as the primary VHA component in advising the Under Secretary for Health on all matters affecting the integrity of research in the protection of human subjects and animals, promoting enhancements in the ethical conduct of research in conformance with regulations and policies and investigating any allegations of research improprieties and research misconduct.

ORCA reports directly to and serves as the primary advisor to the Under Secretary for Health on all matters affecting the integrity of VHA research related to compliance and assurance. ORCA advocates and promotes the application of continuous quality improvement to enhance the ongoing protection of human subjects enrolled in research and welfare of animals used in research. Further, in circumstances involving allegations of potential research impropriety and research misconduct, this office conducts the necessary investigations, and prepares recommendations for remedial and corrective actions. This scope of responsibility is codified in VHA Directive 1058, "Responsibilities of the Office of Research Compliance and Assurance," issued May 23, 2001.

Important to ORCA and the VA are the connections made through ongoing collaboration with the various other federal departments and agencies, and non-governmental organizations that are

responsible for the issues under ORCA's purview. ORCA has close working relationships with the Office for Human Research Protections (OHRP), the Food and Drug Administration (FDA), the Office for Laboratory Animal Welfare (OLAW) and the Office of Research Integrity (ORI), all located in the Department of Health and Human Services. Vitally important relationships with these organizations have helped to ensure that the VA is conducting its activities in a consistent and ethical manner. There is much more that can and will be done to build upon these productive relationships.

Structure

The structure of ORCA includes a central office and five regional offices. The central office is responsible for the overall accomplishment of its mission, while providing direction, guidance and oversight to its five field-based units that routinely perform their delegated operational roles and responsibilities. The central office has eight (8) full time staff; and the four (4) fully activated regional offices are each staffed with four full time staff. Recruitments for the fifth regional office are currently in process.

Each regional office covers a geographical area that encompasses between three and six Veterans Integrated Service Networks (VISNs) and provides support and services on the full scope of ORCA's activities to about 25 VA medical centers (VAMCs) and VA Health care Systems (HCSs). The original four regional offices have been fully staffed since September 2001, and the fifth regional office, which will serve the VAMCs in the three VISNs in the Northeast, will be completely activated by the end of this fiscal year. Each regional office is developing an expertise in a particular area so that it can be an authoritative resource throughout ORCA. For example, in the Southern regional office in Decatur, GA, we have a veterinarian on the staff who collaborates with the VA's chief veterinarian, located at the same VAMC, while the Mid-Atlantic regional office in Washington DC is developing an emphasis in the area of research safety. While the preponderance of ORCA's activities have so far been related to human subject protections, the areas of animal welfare and research safety need to be given greater attention. Also, research misconduct oversight is rapidly evolving as a major issue with the implementation of the new Federal Research Misconduct Policy and the publication in the April 30,2002 Federal Register, that the VA has adopted this policy.

ORCA has established a Field Advisory Committee that meets twice a year to advise on the implementation of its programs. It is composed of VA staff across the full spectrum of operations and research, including representatives from VISNs and VAMCs, such as Associate Chiefs of Staff for Research and Development, Administrative Officers for Research, and Research Compliance Officers.

Philosophy

From the beginning, ORCA has set for itself a course that seeks to promote continuous quality improvement in the responsible conduct of research. Since ORCA is not an entity that has the authority to 'regulate', it is forging a different paradigm. ORCA's philosophy for oversight has been described as the ACE approach. This balanced approach is embodied in the acronym ACE, which refers to ORCA's need to create a culture of Assurance/Assessment, being a Counselor/Cop, and acting as

Educator/Enforcer.

Another key feature has been the interest in developing an emphasis on preventative measures rather than a reliance on the after-the-fact investigation of research improprieties. Research improprieties are violations of the regulations, which the VA has adopted, that govern the responsible conduct of research. These include the "Common Rule" (Title 38 CFR Part 16), various FDA regulations, and certain State regulations for the protection of human subjects enrolled in research. There are also a number of federal regulations that pertain to the welfare of animals, research safety, and the recently promulgated research misconduct policy.

The ongoing intent of ORCA is to continue to shift the philosophy of compliance from a reactive to a proactive mode, wherever possible. ORCA's reactive mode of retrospectively conducting inquiries into allegations of research improprieties will continue as post hoc "for cause" reviews, very similar to those of the Office of the Medical Inspector in its review of allegations of improprieties in clinical situations. Nonetheless, ORCA seeks to emphasize a prospective approach to oversight and surveillance that increasingly relies on prevention of regulatory non-compliance. This requires continuing education that logically will result in a reduced need for remedial education and training.

Product Lines

In accordance with ORCA's scope and derived from its philosophy of proactive operations, ORCA has four primary and four secondary product lines.

The four primary product lines are: 1) Administration of the Assurances Program, 2) Prospective Compliance, 3) Reactive Compliance, and 4) the Training, Education and Development (TED) activity.

The four secondary product lines are: 1) Management of the Adverse Event-Serious Adverse Event processes, 2) Promotion of the Research Compliance Officer (RCO) concept, 3) Liaison with the VA National Ethics Center, and 4) Liaison with the VA Office of Research and Development regarding management of the Human Research Protection Program (HRPP) accreditation contract with the National Committee for Quality Assurance (NCQA).

Primary Product Lines

In March 2000 ORCA assumed responsibility from the Office of Research and Development for the VA Multiple Project Assurance (MPA) contracts for the protection of human subjects. This contract, required by the "Common Rule" is a written document that a VA facility prepares so that it commits itself to fulfill all of the requirements of the federal regulations and VA operational policies and procedures in the protection of human subjects. Today, 111 VAMCs have these "Assurances". At about 40 sites, of the 111, the VAMC, or HCS, rely on the academic affiliate's Institutional Review Board (IRB) to review research protocols to ensure compliance with the provisions of the "Common Rule" and other pertinent regulations.

Since early in 2001, ORCA has worked closely with OHRP to implement a new Federal-Wide Assurance (FWA) program, which is designed to simplify the assurance process. This collaboration with OHRP has worked well, and we have almost completed the conversion of the VA MPA contracts to this

new FWA process. Further, ORCA, under this overall FWA schema, has developed and issued guidance for two sorts of Memoranda of Understanding (MOU). The first set of MOUs allows VAMCs with relatively small research programs to partner with VAMCs having much larger programs and a mature Human Research Protections Program (HRPP). This will enable these smaller programs to capitalize on some economies of scale. Additionally, ORCA has provided VAMCs with guidance and a template for a second MOU between a VAMC and its Academic affiliate, where the VAMC relies upon the affiliate's IRB. These MOUs are important for VAMCs to complete, as they are required by the standards for the accreditation of a HRPP sponsored by the NCQA.

ORCA created and then initiated the prospective compliance product line in September 2001. An ORCA working group, the members drawn from staff at VAMC research programs, has guided the preparation of a Multi Assessment Program or MAP. This MAP has two components: 1) a Self Assessment instrument, and 2) an On-Site review process. The MAP Self-Assessment instrument incorporates checklists for the full scope of ORCA's four areas of responsibility. This instrument includes an introduction to Self Assessment and provides a full list of websites that VAMCs can access to assist them in completing Self Assessments. ORCA has incorporated and distributed the checklist for the HRPP into compact disc (CDROM) containing a compendium of all of the regulations and guidance pertinent to the protection of human subjects. This compendium, also posted on the ORCA website, has cross-linked references to all of the regulations, checklists and accreditation standards for a HRPP mandated by the VA and other federal agencies, including OHRP and FDA. It contains more than 150 documents and they are completely cross-linked to the regulatory source: clicking the internet hyperlink promptly displays the section of the rule or guidance being cited.

During their site visits ORCA's regional office staff orient each VAMC to the MAP Self Assessment process, and provide a list of NCQA's accreditation standards for an HRPP that go beyond the minimum regulatory requirements. The VAMC is also provided written guidance on how to complete a MAP Self Assessment. Research staffs are encouraged to consult with the staff of the VAMC's Quality Assurance Office to assist in conducting a MAP Self Assessment. The ORCA regional office offers to return to do an On-Site MAP review when the VAMC has completed its MAP Self Assessment or before, if the VAMC invites ORCA to return. This MAP is a voluntary program and increasingly VAMCs are recognizing its benefit. Wherever possible, the regional office provides training and education on any subject pertinent to ORCA's mission, requested by the VAMC.

The reactive compliance product line has always been a fundamental ORCA activity. Whenever a VAMC reports a potential or actual research impropriety or ORCA receives a notification from other sources, such as OHRP or the FDA, the ORCA regional office is responsible for follow-up and assistance with the resolution of the issue. The inquiry may be handled by telephone or exchange of correspondence; in some instances the regional office conducts a limited fact finding visit, an on-site Focus Review. If there are more serious systematic problems ORCA selects a Special Inquiry Force Team (SIFT) for an on-site review that lasts for several days. The process follows the general methods

involved in performing a root cause analysis. The SIFT team conducts its work according to a written charter and files its report and recommendations with ORCA central office. The Under Secretary for Health signs and issues the final report and ORCA monitors Action Plans until all of the recommendations have been fully implemented. ORCA then closes the SIFT review with a written notification to conclude the process and after all of the recommendations have been satisfactorily implemented.

ORCA has conducted ten (10) SIFT reviews, two of which are in active status. Among the eight (8) that have now been closed out, one VAMC was in serious regulatory non-compliance, and ORCA placed restrictions on its "Assurance", that took almost a year to resolve. ORCA confers with OHRP when issuing a restriction on a VAMC's "Assurance". The problems ORCA has identified in the SIFT reviews are comparable to, if not identical to, the problems that have been identified by OHRP.

The fourth primary product line is the training, education and development (TED) activity. ORCA has an ongoing working group for this TED activity and the Under Secretary for Health has annually approved the strategic plan for these TED activities. The TED working group has provided guidance in several basic and developmental activities. ORCA has a web site [www.va.gov/ORCA] that continues to grow in importance as a vehicle for identifying important education and training resources. Copies of all of ORCA's fifty or so Information Letters, the ten ALERTS on critical issues, and the minutes of ORCA's Bimonthly Teleconferences are all posted on the website. The website is regularly updated. Also appearing on the website is a Best Practices guidance document n how a VAMC can prepare a standard operating procedures manual for its IRB. ORCA originally issued this as a CD, and we have had many requests for copies from interested parties beyond the VA. The TED working group has also identified sources for training and education of investigators in human subjects protection as required by VA's Office of Research and Development and National Institutes of Heath (NIH). Through collaborative arrangements with several academic institutions that are involved in a project known as CITI (Collaborative IRB Training Initiative), we were able to assist in the preparation of a specific module on research protections in the Department of Veterans Affairs. This CITI program is an optional training vehicle for investigators to be certified in human subjects protection. In addition, all VAMC Directors must complete three training modules on their responsibilities under the FWA that they all sign. Recently, ORCA has, in conjunction with OHRP, begun to distribute CDs to VAMCs and training manuals prepared by the main professional association, Public Responsibility in Medicine and Research (PRIM&R). These are intended for use by investigators and other research staff to help them understand the ethical foundations of the regulatory requirements for the responsible and ethical conduct of research involving human subjects.

ORCA has also presented a VA DAY at the Annual PRIM&R meeting for the past two years and will continue to support these annual forums. In partnership with OHRP and the FDA, ORCA is sponsoring joint conferences and seminars on the protection of human subjects, which occur about six times a year. ORCA's regional offices take the lead for the VA on the seminar's planning committees. Further, over the past year, ORCA has worked with the VISN leadership to conduct one-day intensive

seminars on the various requirements for the responsible conduct of research. The faculty for these seminars, which are targeted for VA's senior executives routinely include representatives from OHRP and FDA. These seminars have broad representation from the leadership of the VISNs and their VAMCs. These seminars, almost complete now, have been well received and the materials distributed are current.

While TED activities assist VA personnel in understanding the responsible conduct of research within the research enterprise, ORCA has not forgotten the veteran who is or might participate in VA research. ORCA has developed a brochure, "I'm a veteran. Should I participate in research?" which was recently unveiled April 10 by the Under Secretary for Health at the bi-monthly meeting of the Veterans' Services Organizations (VSOs). This brochure will help veterans understand their rights as research volunteers and help them decide if they want to participate in a research protocol. ORCA will widely distribute the brochures this month throughout the VA and to the VSOs. The brochure indicates where veterans can make local contact with those knowledgeable about VA research at a VAMC and what it means to volunteer.

Secondary Product Lines

As regards to the four secondary product lines some particular comments are needed to clarify ORCA's role. Management of the Adverse Event/Serious Adverse Event processes was assigned to ORCA in March 2000. Dr. David Weber, Deputy Chief Officer, ORCA, has taken the lead for administering this process and is continuing to bring some 'common sense' to this difficult and complex issue. He processes all serious and unexpected adverse events reported to ORCA, in accordance with regulations and the additional guidance ORCA has provided in its Information Letters. For the past several months he has participated in a working group, under the aegis of OHRP with representation from several other departments and agencies. He chairs an ORCA working group that is charged with simplifying the adverse events reporting issues for research. Further, guidance will soon be provided, which will harmonize with the directions taken by OHRP and, in particular, FDA.

ORCA has been promoting the concept of dedicated quality assurance staff for research activities. About five years ago, VISN # 7 established a Research Assurance and Compliance Officer (RACO) for its research product line, and since then other VISNs have established RACOs, and, some VAMCs have established Research Compliance Officers (RCOs). These individuals play a role in quality assurance and quality improvement management, monitoring compliance with regulations for the responsible conduct of research. These individuals have performed a number of functions such as "audits" of research protocols, routine monitoring of the IRB activities and the conduct of education and training activities. ORCA's Field Advisory Committee recently established a subcommittee to document the level of activity within VAMCs and the VISNs and ascertain what ORCA can do to assist in the further development of these RACO and RCO positions.

ORCA, early on in its existence, established a close liaison with the VA National Ethics Center for the purposes of collaborating on matters concerning the ethical conduct of research. A member of ORCA's central office staff serves on the VA's Ethics Advisory Committee, administered by this Center. It

has been addressing a number of important issues related to research, especially in regard to clarification of some important definitions of what should be included under the umbrella of human subjects research.

ORCA has a direct liaison with the HRPP accreditation program sponsored by National Committee for Quality Assurance (NCQA) and under contract with the VA, through the Office of Research and Development. Until just recently, ORCA has acted in a general advisory capacity, offering its ideas and suggestions. Now that the contractor for this accreditation program, the NCQA, has begun to notify VAMCs it has surveyed of their accreditation statuses, the level of activity for ORCA has significantly increased. NCQA has made determinations of accreditation status at eleven (11) of the 23 sites it has surveyed and has issued notices of "Not Accredited" at three (3) VAMCs and "Accredited with Conditions" at the other eight VAMCs.

These accreditation determinations have been of great concern. ORCA makes immediate contact with the VAMCs that are "Not Accredited" to make a preliminary assessment of the situation. Within 48 hours a Focus Review team, of one or two ORCA staff, is on-site to make a better assessment as to whether human subjects enrolled in the research protocols are adequately protected and determine, as far as possible, whether there has been any medical harm. Also, an evaluation is made as to whether there is any serious or egregious non-compliance with the regulations that are designed to protect human subjects at the VAMC. If so, ORCA may immediately suspend or restrict the VAMC's "Assurance". So far, the three completed Focus Review reports are reassuring, but they are insufficient to make a complete determination of the extent and magnitude of possible regulatory non-compliance.

Each of these VAMCs that received notification of "Not Accredited" were surveyed several months ago by NCQA, and all of them have sent NCQA letters of intent to appeal, within 30 day limit. Filing an appeal with NCQA "freezes" the notification until the NCQA's Appeals Panel considers additional information provided by the VAMC and renders a final decision. ORCA needs in depth and current information about the HRPP activities and has created a Systematic Post-Accreditation Review (SP-AR) to address the situations at VAMCs when NCQA gives a "Not Accredited" designation. ORCA conducts a SP-AR review at the VAMC, the week after the VAMC files its appeal documents with NCQA. The charter for a SP-AR defines the purpose for these on-site reviews performed by a team of several ORCA staff and peer research administrators. The SP-AR is expected to assess the full scope and significance of the issues that relate to the performance of the VAMC's HRPP. The SP-AR report, including recommendations, is available two weeks after the team completes its on-site review. The first SP-AR report is due the end of this week.

During the course of the on-site review, serious and egregious non-compliance with the regulations that protect human research subjects may become apparent. If so, ORCA may issue a suspension or restriction on the VAMC's "Assurance". While no SP-AR reports have been completed, ORCA has issued a restriction on the "Assurance" at one VAMC that was "Not Accredited" for serious, but not egregious, non-compliance with several provisions of the "Common Rule". When the SP-AR report is completed ORCA decides on the next steps and elicits an Action Plan from the VAMC that has to

substantially address the recommendations. Other notifications will need to be made, as appropriate, to other regulatory agencies such as OHRP and FDA. Eventually, when the Recommendations have all been fully implemented to ORCA's satisfaction, the Office of Research and Development will be notified. This will signal that consideration might be given to a new review of the VAMC's HRPP through the NCQA accreditation program.

Conclusion.

In summary, in the three years since the Under Secretary for Health announced the establishment of this office, ORCA has exerted considerable time, thought and energy to defining its scope, creating its structure, articulating its philosophy, and delineating its product lines. The 'die has been cast' to firmly establish ORCA as the primary office within the VA for oversight of the VA research enterprise in regard to the responsible conduct of research. This role and responsibility has to be fulfilled in collaboration with the other VA offices, the relevant other federal departments and agencies, and non-governmental organizations. Over the next few years the foundation that has been established in ORCA will allow for the construction of an even more robust research enterprise where the rights of human subjects will be continuously protected.

Again, I appreciate the invitation to discuss these important issues with you, and I will be pleased to try and answer any questions you might have.